Remarks

Claims 1-20 are pending. Claims 1-12 have been withdrawn from consideration as drawn to a non-elected group. Claims 1 and 8 to 20 have been amended.

Applicants acknowledge that the restriction requirement has been made final. To preserve the right of rejoinder, Applicants have amended method claims 1 and 8 to 12 to be commensurate in scope to the product claims that are under consideration.

Applicants thank the Examiner for her comments regarding claims 14 and 20. Applicants believe that the amendments presented herein respond to the concerns raised in the Examiner's comments.

Claim Rejections under 35 U.S.C. § 112

Claims 13, 14, 15, 19 and 20 stand rejected under 35 U.S.C. § 112 as indefinite because the description of the second oligonucleotide in claim 13 was internally inconsistent because the lengths of the second oligonucleotides were inconsistent with the additive lengths based on the limitations of claim 13 and the lengths of the sequences identified by SEQ ID numbers in claims 14, 15, 19 and 20. Applicants thank the Examiner for her careful reading of the claims. Applicants have amended claim 13 to describe the second oligonucleotide as one consisting of 19 to 25 bases that contains contiguous bases 1 to 18 of SEQ ID NO:24 and optionally three to seven bases 5' to the contiguous bases 1 to 18 of SEQ ID NO:24 and/or optionally one base 3' to the contiguous bases 1 to 18 of SEQ ID NO:24. Applicants believe that this amendment removes the source of confusion in pending claim 13. Amended claims 14, 15, 19 and 20 recite oligonucleotide embodiments consistent with the limitations of amended claim 13. The sequences of SEQ ID numbers 21, 22, 23, and 24 have been aligned as shown below to assist the Examiner in examining the claims.

SEQ No.	Sequence	Length
24	gaacggaaaggcctttcgg	19

21	gcaagtcgaacggaaaggcctttcg	25
22	caagtcgaacggaaaggcctttcg	24
23	gtcgaacggaaaggcctttcgg	22

Applicants believe that these amendments overcome the rejections raised under 35 U.S.C. § 112 and request reconsideration of amended claims 13, 14, 15, 19 and 20.

Claim Rejections under 35 U.S.C. § 102

Claims 16 and 17 stand rejected under 35 U.S.C. § 102(b) as being anticipated by GenBank accession no. X53896, GI (04 Sept 1991) which teaches the partial nucleic acid sequence of 16S rRNA from *Mycobacterium cookii*.

To be anticipated, there must be no difference between the claimed invention and the reference disclosure, as viewed by a person of ordinary skill in the field of the invention. *Scripps Clinic & Res. Fndn. v. Genentec, Inc.*, 927 F.2d 1565, 18 U.S.P.Q.2d 1001, 1010, 18 U.S.P.Q.2d 1896 (Fed. Cir. 1991).

Claim 16 has been amended to delete the phrase "having a sequence" making the independent claim read "... one or more oligonucleotides selected from the group consisting of SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, and SEQ ID NO:24." Dependent claim 17 has been amended to read "... further containing an oligonucleotide consisting of SEQ ID NO:11." Based on these amendments, Applicants respectfully submit that a person of ordinary skill in the field of molecular biology would not view the teachings of a partial 16S rRNA sequence from *M. cookii* as having no difference from a kit containing the specific oligonucleotides named in amended claims 16 and 17. Therefore, Applicants respectfully request withdrawal of the rejections of claims 16 and 17 under 35 U.S.C. § 102(b).

Claim Rejections under 35 U.S.C. § 103

Claims 16 to 18 stand rejected under 35 U.S.C. § 103(a) based on the teachings of Kazda et al. (*Int. J. Syst. Bacteriol.*, 1990, 40(3): 217-23) in view of GenBank accession no. X53896, GI (04 Sept 1991). The "kit" claims were interpreted broadly and treated as a recitation of intended use. Kazda et al. was cited for teaching isolated nucleic acid molecules that are the product of long range reverse transcript generated sequences of 16S rRNA of *M. cookii*, which, because the procedure would have resulted in multiple copies of double stranded molecules, was interpreted to provide a reaction product that would have had multiple first and second oligonucleotide molecules. Because Kazda et al. do not teach a sequence selected from the group consisting of SEQ ID Nos. 21-24, it was combined with the teachings of GenBank accession no. X53896, which encompasses the sequences of SEQ ID Nos. 21-24 in selected regions of the X53896 sequence and the complement of SEQ ID NO:11 in a selected region of the X53896 sequence. The sequences of claims 17 and 18 were interpreted broadly as requiring only small portions of the recited sequences, e.g., as few as two nucleotides of SEQ ID NO:11.

Factual predicates underlying a determination of *prima facie* obviousness include the scope and content of the prior art, the differences between the prior art and the claimed invention, and the level of ordinary skill in the art. *Graham v. John Deere Co.*, 383 U.S. 1, 17-18 (1966); *In re Rouffet*, 149 F.3d 1350, 47 U.S.P.Q.2d 1453, 1455 (Fed. Cir. 1998), *citing Monarch Knitting Mach. Corp. v. Sulzer Morat GmbH*, 139 F.3d. 877, 881, 45 U.S.P.Q.2d 1977, 1981 (Fed. Cir. 1998); *In re Kotzab*, 217 F.3d 1365, 1369 (Fed. Cir. 2000). Analysis under §103 requires consideration of whether: (1) the prior art would have suggested to those of ordinary skill in the art that they should make the claimed composition; and (2) the prior art would also have revealed that in so making, those of skill in the art would have had a reasonable expectation of success. *In re Vaeck*, 947 F.2d 488, 20 U.S.P.Q.2d 1438 (Fed. Cir. 1991). When a rejection under §103 depends on a

combination of prior art references, there must be some teaching, suggestion, or motivation to combine the references. *In re Rouffet*, 47 U.S.P.Q.2d 1453, 1456 (Fed. Cir. 1998).

Applicants have amended claims 16-18 as described above, which make clear that certain selected oligonucleotides identified by SEQ ID Nos. are included in the claimed kit compositions. Thus, the broad interpretations of the claims used in making these rejections do not apply to the amended claims. The cited prior art references provide sequence information on large portion(s) of the 16S rRNA sequence of *M. cookii*, e.g., the GenBank X53896 sequence encompasses a 1459 nucleotide region. The prior art would not have suggested to a person of ordinary skill in the art of molecular biology that they should make the claimed compositions that included these selected sequences, nor would the cited prior art have revealed that the person of ordinary skill would have had a reasonable expectation of success at arriving at the claimed compositions. Therefore, Applicants respectfully request that the rejections under §103 of claims 16-18 be withdrawn and amended claims 16-18 be allowed.

Claims 13-15 and 19-20 stand rejected under 35 U.S.C. § 103(a) based on the teachings of Hogan et al. (US 5677128) in view of GenBank accession no. X53896, GI (04 Sept 1991), and further in view of McAllister et al. (US 5908744). Hogan et al. was cited for teaching probes that target the 16S rRNA region of *Mycobacterium* species, probes of about 15 to 50 bases, examples of single species and genus specific probes, kits, and for providing guidance on the selection of oligonucleotides (quoting from column 6, line 48 to column 7, line 13). But Hogan et al. do not teach oligonucleotides as described in claim 13 and the GenBank X53896 sequence was cited as teaching the *M. cookii* partial 16S rRNA sequence that encompasses the sequences of the specified SEQ ID numbers (for claim 16), particularly when interpreted broadly (for claims 14, 15, 19 and 20), e.g., to require only small portions of the recited sequences identified by SEQ ID numbers.

Applicants have amended claims 13-15 and 19-20 to more particularly describe the claimed compositions, and respectfully submit that these amendments remove any basis for the broad interpretations of the sequences that were used in making these rejections. Thus, the large sequence of the GenBank reference do not teach or suggest the claimed compositions, even if combined with the teachings of Hogan et al. Applicants note that the claimed sequences of SEQ ID Nos. 21, 22, 23 and 24 fail to comply with the specific guidance for the selection of oligonucleotides provided by Hogan et al. that was quoted in the rejection. That is, Hogan et al. state that one should select oligonucleotide sequences that avoid long A and T rich sequences and avoid extensive self complementarity. The sequences of SEQ ID Nos. 21, 22, 23 and 24, however, all include A-rich and T-rich sequences (e.g., the 19 base sequence of SEQ ID NO:24 includes 5 A and 3 T bases, making it about 42% AT rich) and the individual oligonucleotide sequences contain contiguous sequences that are self complementary as illustrated by the hairpin configuration of SEQ ID NO:24 shown below in which self complementary bases are in bold.

5'g a a **c** g **g a a a g g**
3' **g** g **c t t t c c**

A person of ordinary skill in the art of molecular biology provided with the guidance of Hogan et al. and given the relatively large sequence taught by the GenBank X53896 sequence from which to choose oligonucleotide sequences would not have been lead to select those of SEQ ID Nos. 21-24 which are relatively AT-rich and contain self complementary regions. The teachings of McAllister et al., which were cited for teaching compositions and kits that use promoter primers that include a T7 bacteriophage promoter and use of such primers for detection of *Mycobacterium*, do not remedy the deficiencies of combining the first two references. That is, a person of ordinary skill in the art would not have been motivated to select the oligonucleotide sequences as claimed in amended claims 13-15 and 19-20 based on the combined teachings of Hogan et al., GenBank X53896 and McAllister et al.

Therefore, Applicants respectfully request allowance of amended claims 13-15 and 19-20.

Claims 13-15 and 19-20 stand rejected under 35 U.S.C. § 103(a) based on the teachings of McAllister et al. (US 5908744) in view of GenBank accession no. X53896, and further in view of Buck et al. (*BioTechniques*, 1999, 27:528-36). The teachings of McAllister et al. and GenBank X53896 were applied substantially as summarized above, but McAllister et al. does not teach a 19 to 25 base oligonucleotide that contains 18 contiguous bases of SEQ ID NO:24. The McAllister reference was combined with the GenBank X53896 reference because the latter teaches a 1459 base 16S rRNA sequence that encompasses the claimed sequences, when the claims are broadly interpreted, as described above. Buck et al. was cited to provide "evidence of the equivalence of primers."

Because the teachings of McAllister et al. and the GenBank X53896 reference were discussed above with regard to rejections under §103, Applicants respectfully refer the Examiner to the earlier discussions of those references.

Applicants strongly disagree that Buck et al. provide "evidence of the equivalence of primers" and with the conclusion "that every primer would have a reasonable expectation of success" based on the arguments that follow. The teachings of Buck et al. must be assessed in the context of the system used by Buck et al. in their survey of DNA sequencing primers. First, Buck et al. selected and provided an optimal test sequence that was "previously shown to contain no segments that affect sequence ladder extension" and " lacking obstacles to sequence extension" which was extensively purified (page 529, column 3, and page 530, column 2, "Test Template and Preparation"). See also page 535, end of column 2: "the plasmid template was selected for absence of sequence extension obstacles and purified by double banding in CsCl-ethidium bromide isopycnic density gradients. Therefore, this template was extremely pure and optimal for sequencing." Second, Buck et al.

provided this specially selected test sequence to participants in specialized laboratories (85% of which "provide sequencing services") and requested that they select and submit "up to three" of their "best primers" for the test sequence (page 529, column 3, and page 530, column 3 "Participant Profiles"). Buck et al. synthesized the submitted "best primers" along with 95 control primers which were based on sequential sequences at 3-bp intervals on the optimized test sequence (page 530, column 1, first full paragraph). The primers were highly purified (page 530, column 1, last paragraph, and page 535, column 2, last paragraph) and tested individually in DNA sequencing reactions by using the highly purified specially selected test DNA under specific conditions (see page 530, column 2-3 "DNA Sequence Analysis"). Fourth, the analysis of results included *elimination of data* that contained "ambiguities" (page 530, column 3, first paragraph: "the raw data was trimmed to remove 5' and 3' ambiguous sequences, so that the first and last 25 nt contained no ambiguities"). In the discussion of the "Sequencing Performance of the Primers" (page 533, column 1), Buck et al. report that all of the "submitted primers functioned extremely well" and "almost all of the control primers functioned very well" or generated "very respectable data" (page 533, column 2). Despite these laudatory conclusions, errors or ambiguities were reported (page 533, column 1-2, text under Figure 2, and Table 3, footnote 1). Buck et al. also state that varying only one condition ("Old Rhodamines vs. dRhodamines" at page 535, column 1) changed the performance of the primers. Buck et al. acknowledge that their tests were performed by using a specially selected test sequence, highly purified target DNA and primers, and "tightly controlled conditions" and that different results may be obtained by using different sequences or conditions (text spanning page 535, column 3 to page 536, column 1).

A reference must be considered for all that it teaches. Applicants note that the participants of the study disclosed by Buck et al., due to their employment in specialized laboratories that, e.g., provide sequencing services, may have much greater skill than a person of ordinary skill in the art of molecular biology. And Buck et al. teach: (1) using a specially selected target sequence that contains

no impediments to primer extension for design and selection of primers, (2) individually testing highly purified primers by using a highly purified optimal test sequence under tightly controlled DNA sequencing conditions, and (3) data analysis that selectively eliminates certain portions of data that include ambiguities. The first two parameters minimize the potential of a primer performing poorly and the third parameter eliminates data that contains ambiguous results, thereby minimizing the frequency of errors in the overall results to arrive at the conclusion stated at page 535. Instead, a more accurate conclusion based on the study of Buck et al. might be that primers performed well when they were designed by using a specially selected target DNA that had been shown to lack obstacles to primer extension, when the primers were tested individually using the highly purified target DNA as a template in sequencing reactions performed under specific and tightly controlled conditions, and when the raw data was manipulated to selectively remove portions that contain ambiguities. This more accurate interpretation of the study contrasts to the statement that "every primer would have a reasonable expectation of success" which was relied upon in making these rejections under § 103(a).

Applicants, therefore, respectfully submit that the compositions of amended claims 13-15 and 19-20 would not have been suggested to a person of ordinary skill in the art of molecular biology based on the teachings of the cited references because (1) McAllister et al. do not teach the sequences identified in the claims, (2) the GenBank record does not teach the selected sequences claimed because the amended claims should not be so broadly interpreted, and (3) the teachings of Buck et al. are limited to a specialized test system used in that study which selectively eliminated data before arriving at its conclusions. In view of the above arguments, Applicants request reconsideration of claims 13-15 and 19-20 as amended herein.

Conclusion

In view of the foregoing amendments and remarks, the Applicants respectfully submit that the claims, as amended, are patentable and in condition for allowance. Accordingly, withdrawal of the

rejections and allowance of the application is earnestly solicited. The undersigned has made a good-faith effort to address all the points raised in this Office action and to place the claims in condition for allowance. However if minor matters remain that could be resolved by telephone interview, the Examiner is invited to contact the undersigned at the number shown below.

No fee is believed due in connection with this timely response (October 28th being on a weekend). If Applicants are incorrect, authorization is hereby provided to debit required fees from Deposit Account No. 07-0835 maintained by Gen-Probe Incorporated.

Respectfully Submitted,

Dated: October 30, 2006

By: /Christine A. Gritzmacher/
Christine A. Gritzmacher
Attorney of Record, Reg. No. 40,627

GEN-PROBE INCORPORATED
Patent Department
10210 Genetic Center Drive
San Diego, CA 92121

Tel.: (858) 410-8926
FAX: (858) 410-8928